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|---|---|---|
| NEWS 1 | | Web Page URLs for STN Seminar Schedule - N. America |
| NEWS 2 | | "Ask CAS" for self-help around the clock |
| NEWS 3 | SEP 09 | CA/CAplus records now contain indexing from 1907 to the present |
| NEWS 4 | DEC 08 | INPADOC: Legal Status data reloaded |
| NEWS 5 | SEP 29 | DISSABS now available on STN |
| NEWS 6 | OCT 10 | PCTFULL: Two new display fields added |
| NEWS 7 | OCT 21 | BIOSIS file reloaded and enhanced |
| NEWS 8 | OCT 28 | BIOSIS file segment of TOXCENTER reloaded and enhanced |
| NEWS 9 | NOV 24 | MSDS-CCOHS file reloaded |
| NEWS 10 | DEC 08 | CABA reloaded with left truncation |
| NEWS 11 | DEC 08 | IMS file names changed |
| NEWS 12 | DEC 09 | Experimental property data collected by CAS now available in REGISTRY |
| NEWS 13 | DEC 09 | STN Entry Date available for display in REGISTRY and CA/CAplus |
| NEWS 14 | DEC 17 | DGENE: Two new display fields added |
| NEWS 15 | DEC 18 | BIOTECHNO no longer updated |
| NEWS 16 | DEC 19 | CROPU no longer updated; subscriber discount no longer available |
| NEWS 17 | DEC 22 | Additional INPI reactions and pre-1907 documents added to CAS databases |
| NEWS 18 | DEC 22 | IFIPAT/IFIUDB/IFICDB reloaded with new data and search fields |
| NEWS 19 | DEC 22 | ABI-INFORM now available on STN |
| NEWS 20 | JAN 27 | Source of Registration (SR) information in REGISTRY updated and searchable |
| NEWS 21 | JAN 27 | A new search aid, the Company Name Thesaurus, available in CA/CAplus |
| NEWS 22 | FEB 05 | German (DE) application and patent publication number format changes |
| NEWS 23 | MAR 03 | MEDLINE and LMEDLINE reloaded |
| NEWS 24 | MAR 03 | MEDLINE file segment of TOXCENTER reloaded |
| NEWS 25 | MAR 03 | FRANCEPAT now available on STN |

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|---|---|
| NEWS EXPRESS | MARCH 5 CURRENT WINDOWS VERSION IS V7.00A, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 3 MARCH 2004 |
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| NEWS INTER | General Internet Information |
| NEWS LOGIN | Welcome Banner and News Items |
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FILE 'HOME' ENTERED AT 13:17:17 ON 25 MAR 2004

=> FIL MEDLINE BIOSIS EMBASE CA SCISEARCH
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21

FILE 'MEDLINE' ENTERED AT 13:17:23 ON 25 MAR 2004

FILE 'BIOSIS' ENTERED AT 13:17:23 ON 25 MAR 2004
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FILE 'EMBASE' ENTERED AT 13:17:23 ON 25 MAR 2004
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FILE 'SCISEARCH' ENTERED AT 13:17:23 ON 25 MAR 2004
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=> s ((emap (n) II) or endothelial monocyte activating polypeptide?)
L1          451 ((EMAP (N) II) OR ENDOTHELIAL MONOCYTE ACTIVATING POLYPEPTIDE?)

=> s antisense or anti (n) sense or (comple? (2n) (oligonucl? or nucl?))
   4 FILES SEARCHED...
L2       220323 ANTISENSE OR ANTI (N) SENSE OR (COMPLE? (2N) (OLIGONUCL? OR
                NUCL?))

=> s l1 and l2
L3            8 L1 AND L2

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4            8 DUP REM L3 (0 DUPLICATES REMOVED)

=> s l4 and py<=1998
   2 FILES SEARCHED...
L5            0 L4 AND PY<=1998

=> d hsi
L5 HAS NO ANSWERS
L1          451 SEA ((EMAP (N) II) OR ENDOTHELIAL MONOCYTE ACTIVATING POLYPEPTI
                DE?)
L2       220323 SEA ANTISENSE OR ANTI (N) SENSE OR (COMPLE? (2N) (OLIGONUCL?
                OR NUCL?))
L3            8 SEA L1 AND L2
L4            8 DUP REM L3 (0 DUPLICATES REMOVED)
L5            0 SEA L4 AND PY<=1998


=> d his

     (FILE 'HOME' ENTERED AT 13:17:17 ON 25 MAR 2004)
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     FILE 'MEDLINE, BIOSIS, EMBASE, CA, SCISEARCH' ENTERED AT 13:17:23 ON 25
     MAR 2004
L1           451 S ((EMAP (N) II) OR ENDOTHELIAL MONOCYTE ACTIVATING POLYPEPTIDE
L2        220323 S ANTISENSE OR ANTI (N) SENSE OR (COMPLE? (2N) (OLIGONUCL? OR N
L3             8 S L1 AND L2
L4             8 DUP REM L3 (0 DUPLICATES REMOVED)
L5             0 S L4 AND PY<=1998

=> s (inhib? or reduc? (s) l1)
L6       5763902 (INHIB? OR REDUC? (S) L1)

=> s ((inhib? or reduc?) (s) l1)
L7            87 ((INHIB? OR REDUC?) (S) L1)

=> dup rem l7
PROCESSING COMPLETED FOR L7
L8            33 DUP REM L7 (54 DUPLICATES REMOVED)

=> s l8 and py<=1999
   2 FILES SEARCHED...
L9            12 L8 AND PY<=1999

=> d his

     (FILE 'HOME' ENTERED AT 13:17:17 ON 25 MAR 2004)

     FILE 'MEDLINE, BIOSIS, EMBASE, CA, SCISEARCH' ENTERED AT 13:17:23 ON 25
     MAR 2004
L1           451 S ((EMAP (N) II) OR ENDOTHELIAL MONOCYTE ACTIVATING POLYPEPTIDE
L2        220323 S ANTISENSE OR ANTI (N) SENSE OR (COMPLE? (2N) (OLIGONUCL? OR N
L3             8 S L1 AND L2
L4             8 DUP REM L3 (0 DUPLICATES REMOVED)
L5             0 S L4 AND PY<=1998
L6       5763902 S (INHIB? OR REDUC? (S) L1)
L7            87 S ((INHIB? OR REDUC?) (S) L1)
L8            33 DUP REM L7 (54 DUPLICATES REMOVED)
L9            12 S L8 AND PY<=1999

=> s l9 or l4
L10           20 L9 OR L4

=> dup rem l10
PROCESSING COMPLETED FOR L10
L11           20 DUP REM L10 (0 DUPLICATES REMOVED)

=> d l11 1-20 ibib abs

L11  ANSWER 1 OF 20  CA  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:        140:162369  CA
TITLE:                   Antisense oligonucleotides for inactivation
                         of mismatch repair gene to generate cell lines with
                         enhanced antibody production and improved growth
                         characteristics
INVENTOR(S):             Grasso, Luigi; Kline, J. Bradford; Nicolaides,
                         Nicholas C.; Sass, Philip M.
PATENT ASSIGNEE(S):      Morphotek, Inc., USA
SOURCE:                  PCT Int. Appl., 47 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:
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| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004009782 | A2 | 20040129 | WO 2003-US22743 | 20030721 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-397027P P 20020719

AB The use of mismatch repair (MMR) defective antibody producer cells offers a method to generate subclone variants with elevated protein production such as antibodies. Using MMR defective cells and animals, new cell lines and animal varieties with novel and useful properties such as enhanced protein production can be generated more efficiently than by relying on the natural rate of mutation. These methods are useful for generating genetic diversity within host cells to alter endogenous genes that can yield increased titer levels of protein production By employing this method, two genes were discovered whose suppressed expression is associated with enhanced antibody production Suppressed expression of these genes by a variety of methods leads to increased antibody production for manufacturing as well as strategies for modulating antibody production in immunol. disorders. Moreover, the suppression of these two genes in host cells can be useful for generating universal high titer protein production lines.

L11 ANSWER 2 OF 20 CA 

ACCESSION NUMBER: 138:50892 CA

TITLE: Protein and cDNA sequences of a novel human **endothelial monocyte-activating polypeptide** II-like protein 10.01 and therapeutic use thereof

INVENTOR(S): Mao, Yumin; Xie, Yi

PATENT ASSIGNEE(S): Bode Gene Development Co., Ltd., Shanghai, Peop. Rep. China

SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 36 pp. CODEN: CNXXEV

DOCUMENT TYPE: Patent

LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| CN 1339467 | A | 20020313 | CN 2000-119653 | 20000821 |

PRIORITY APPLN. INFO.: CN 2000-119653 20000821

AB The invention provides protein and cDNA sequences of a novel 10.01-kilodalton human protein, designated as "**endothelial monocyte-activating polypeptide** II-like protein 10.01", which has similar expression pattern with known **endothelial monocyte-activating polypeptide** II. The invention relates to expression of **endothelial monocyte-activating polypeptide** II-like protein 10.01 in E.coli BL21(DE3)plySs transfected with plasmid pET-28(+). The invention also relates to preparation of antibody against **endothelial monocyte-activating polypeptide** II-like protein 10.01. The invention further relates to the uses of the **endothelial monocyte-activating polypeptide** II-like

protein 10.01 fragment as probes in diagnosis, and in treatment of **endothelial monocyte-activating polypeptide** II-like protein 10.01-related diseases (such as inflammation, neoplasm, immune disorder).

L11 ANSWER 3 OF 20 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 135:268250 CA
TITLE: Human **endothelial monocyte activating polypeptide** II 62 and its cDNA and therapeutic use thereof
INVENTOR(S): Mao, Yumin; Xie, Yi
PATENT ASSIGNEE(S): Shanghai Biowindow Gene Development Inc., Peop. Rep. China
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001068874 | A1 | 20010920 | WO 2001-CN177 | 20010226 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CN 1313330 | A | 20010919 | CN 2000-114915 | 20000315 |

PRIORITY APPLN. INFO.: CN 2000-114915 A 20000315

AB The invention provides cDNA sequences of a novel human **endothelial monocyte activating polypeptide** II 62 (62 kDa) cloned from human embryonic brain. The invention also relates to constructing the cloned gene expression vectors to prepare its recombinant protein using E.coli cells or eukaryotic cells. Methods of expressing and preparing the above recombinant protein and its antibody are described. Methods of using related gene or protein products for the treatment of various kinds of diseases, such as cancer, blood diseases, HIV infection, immune diseases, mammalian development diseases, and inflammation are also disclosed. Methods for screening for related analogs, agonists, inhibitors and antagonists to be used as therapeutic drugs are also described.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 20 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 135:132441 CA
TITLE: Use of **EMAP II** receptor antagonist composition for treating pulmonary hypertension, and screening methods
INVENTOR(S): Schwarz, Margaret
PATENT ASSIGNEE(S): Children's Hospital, USA
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001052879 | A1 | 20010726 | WO 2001-US748 | 20010110 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2001031738 | A1 | 20011018 | US 2000-738685 | 20001215 |
| EP 1248641 | A1 | 20021016 | EP 2001-903010 | 20010110 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| US 2003039652 | A1 | 20030227 | US 2002-274788 | 20021021 |

| | | | |
|---|---|---|---|
| PRIORITY APPLN. INFO.: | US 2000-177008P | P | 20000119 |
| | US 2000-197492P | P | 20000417 |
| | US 2000-738685 | A1 | 20001215 |
| | WO 2001-US748 | W | 20010110 |

AB A method of treating pulmonary hypertension comprises inhibiting **EMAP II** activity by an amount effective to treat the pulmonary hypertension (e.g., in the lungs and more particularly in the pulmonary vasculature). Pharmaceutical formulations useful for carrying out the methods (e.g., an antibody that specifically binds to **EMAP II** in a pharmaceutically acceptable carrier) and screening techniques useful for identifying addnl. compds. that can be used for carrying out such methods are also disclosed.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 5 OF 20 CA 

| | |
|---|---|
| ACCESSION NUMBER: | 135:71286 CA |
| TITLE: | Methods of facilitating vascular growth in cardiac muscle by inhibiting **EMAP II**, and methods for the production of recombinant **EMAP II** |
| INVENTOR(S): | Schwarz, Margaret |
| PATENT ASSIGNEE(S): | Children's Hospital Research Institute, USA |
| SOURCE: | PCT Int. Appl., 22 pp.<br>CODEN: PIXXD2 |
| DOCUMENT TYPE: | Patent |
| LANGUAGE: | English |
| FAMILY ACC. NUM. COUNT: | 1 |

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001047518 | A1 | 20010705 | WO 2000-US33467 | 20001208 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2001041680 | A1 | 20011115 | US 2000-733306 | 20001208 |

| | | | |
|---|---|---|---|
| PRIORITY APPLN. INFO.: | US 1999-171874P | P | 19991223 |
| | US 2000-197558P | P | 20000417 |
| | US 2000-231759P | P | 20000912 |

US 2000-241138P P 20001017

AB A method of facilitating vascular growth in cardiac muscle of a subject in need of such treatment comprises inhibiting **EMAP II** activity in said subject by an amount effective to stimulate vascular growth in said cardiac muscle. The inhibiting step may be carried out by any suitable means, such as: By administering a compound (e.g., an antibody) that specifically binds to **EMAP II** to said subject in an amount effective to stimulate vascular growth in said cardiac muscle; by downregulating **EMAP II** expression in said subject by an amount effective to stimulate vascular growth in said cardiac muscle (e.g., by administration of an **antisense** oligonucleotide); or by administering an **EMAP II** receptor antagonist to said subject in an amount effective to stimulate vascular growth in said cardiac muscle.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 6 OF 20 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 135:294008 CA
TITLE: Antibody-coated adsorbents, column system having the adsorbents for hemodialysis or plasmapheresis, and therapy using the system
INVENTOR(S): Dunzendorfer, Udo
PATENT ASSIGNEE(S): Germany
SOURCE: Jpn. Kokai Tokkyo Koho, 31 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 2001276217 | A2 | 20011009 | JP 2000-102606 | 20000404 |

PRIORITY APPLN. INFO.: JP 2000-102606 20000404

AB The adsorbents, useful for removing pathogenic factors from plasma or tissues, are coated with antibodies to TNF, TNF metabolites, TNF transport proteins, or TNF fragments. The adsorbents may be addnl. coated with monoclonal or polyclonal antibodies to pathogenic factors such as cold agglutinins, HLA antigens, hepatitis virus antigens, β2-microglobulins, bacterial toxins, etc. A column system having the adsorbents and clin. use of the system are also claimed. Selective removal of these pathogens, antigens, proteins, etc. leaves all normal plasma components unchanged and obviates the need for supplementation of the plasma with these components. Suitable substrates include polymers, polymer-coated metals, glass, cellulose, agar, Sepharose, etc. Thus, dextran sulfate-induced colitis was successfully treated by plasmapheresis coupled with adsorbents coated with anti-TNF-α antibody. Addnl. coating of the adsorbents with anti-protein A antibody enhances the effect.

L11 ANSWER 7 OF 20 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 133:218354 CA
TITLE: Mit1/Lb9 and Copg2, new members of mouse imprinted genes closely linked to Peg1/Mest
AUTHOR(S): Lee, Y. J.; Park, C. W.; Hahn, Y.; Park, J.; Lee, J.; Yun, J. H.; Hyun, B.; Chung, J. H.
CORPORATE SOURCE: Department of Biological Sciences, Korea Advanced Institute of Science and Technology, Taejon, S. Korea
SOURCE: FEBS Letters (2000), 472(2,3), 230-234
CODEN: FEBLAL; ISSN: 0014-5793
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Two mouse genes, Mit1/Lb9 and Copg2, linked to Peg1/Mest on mouse chromosome 6, were identified to be imprinted maternally and paternally, resp. Mit1/Lb9 encoding untranslated transcripts resides within the intron 20 of Copg2. The gene is maternally imprinted in adult mouse brain, partially imprinted in other tissues. Copg240 kb genomic region, being expressed ubiquitously in mouse tissues with a partial imprinting pattern in embryos, neonates, and adult brain in contrast to maternally imprinted human COPG2. In addition, we identified an **antisense** transcript of Copg2, Copg2AS, which overlaps 3'-UTRs of Copg2 and Peg1/Mest. The Copg2AS transcript is maternally imprinted in embryos, neonates, and adult tissues.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 8 OF 20 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 130:187193 CA
TITLE: Aqueous aerosol preparations containing biologically active macromolecules and method for their production
INVENTOR(S): Lamche, Herbert; Meade, Christopher John Montague; Zierenberg, Bernd
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma KG, Germany
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9907340 | A1 | 19990218 | WO 1998-EP4803 | 19980731 |
| W: AU, BG, BR, BY, CA, CN, CZ, EE, HU, ID, IL, JP, KR, KZ, LT, LV, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| DE 19733651 | A1 | 19990218 | DE 1997-19733651 | 19970804 |
| AU 9891577 | A1 | 19990301 | AU 1998-91577 | 19980731 |
| AU 753673 | B2 | 20021024 | | |
| EP 1003478 | A1 | 20000531 | EP 1998-943814 | 19980731 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| BR 9811827 | A | 20000815 | BR 1998-11827 | 19980731 |
| EE 200000065 | A | 20001016 | EE 2000-20000006519980731 | |
| JP 2001513492 | T2 | 20010904 | JP 2000-506934 | 19980731 |
| NZ 503160 | A | 20011221 | NZ 1998-503160 | 19980731 |
| ZA 9806931 | A | 19990705 | ZA 1998-6931 | 19980803 |
| NO 2000000553 | A | 20000403 | NO 2000-553 | 20000203 |
| US 2003064032 | A1 | 20030403 | US 2002-288770 | 20021106 |

PRIORITY APPLN. INFO.: DE 1997-19733651 A 19970804
WO 1998-EP4803 W 19980731
US 2000-497696 B1 20000203

AB Aqueous aerosol prepns. containing biol. active macromols. such as insulin are provided for producing inhalable aerosols without propellant gases by use of the Respimat nebulizer (described in WO 97/12687). This nebulizer delivers controlled 10-50-μL doses of highly concentrated macromol. solns. with mean droplet sizes of 3-10 μm at high pressure through an orifice of hydraulic diameter 1-12 μm by a spring-driven mechanism under conditions which do not inactivate macromols. The viscosity of the concentrated solution of active agent should be ≤1600 + 10-6 Pa s to provide adequate aerosolization. Thus, the reservoir of a Respimat was filled

with a solution containing 50 mM tri-Na citrate, 150 mM NaCl, and 5 mg interferon
ω/mL (pH 5.5), and 12.9 μL of the solution was expelled at 28 L/min into a trap. Recovery of active interferon ω from the trap in 3 trials was 84, 77, and 98% by ELISA and 54, 47, and 81% by bioassay, resp.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 9 OF 20 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 1999208135 EMBASE
TITLE: Precursor of pro-apoptotic cytokine modulates aminoacylation activity of tRNA synthetase.
AUTHOR: Sang Gyu Park; Keum Hee Jung; Jong Sang Lee; Yeong Joon Jo; Motegi H.; Kim S.; Shiba K.
CORPORATE SOURCE: S. Kim, Dept. of Biological Science, Sung Kyun Kwan University, 300 Chunchundong, Jangangu, Suwon, Kyunggido 440-746, Korea, Republic of. shkim@yurim.skku.ac.kr
SOURCE: Journal of Biological Chemistry, (11 Jun 1999) 274/24 (16673-16676).
Refs: 28
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB **Endothelial monocyte activating polypeptide** II (EMAPII) is a cytokine that is specifically induced by apoptosis. Its precursor (pro-EMAPII) has been suggested to be identical to p43, which is associated with the multi- tRNA synthetase complex. Herein, we have demonstrated that the N-terminal domain of pro-EMAPH interacts with the N-terminal extension of human cytoplasmic arginyl-tRNA synthetase (RRS) using genetic and immunoprecipitation analyses. Aminoacylation activity of RRS was enhanced about 2.5-fold by the interaction with pro-EMAPH but not with its N- or C- terminal domains alone. The N-terminal extension of RRS was not required for enzyme activity but did mediate activity stimulation by pro-EMAPH. Pro-EMAPH **reduced** the apparent K(m) of RRS to tRNA, whereas the k(cat) value remained unchanged. Therefore, the precursor of EMAPII is a multi-functional protein that assists aminoacylation in normal cells and releases the functional cytokine upon apoptosis.

L11 ANSWER 10 OF 20 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 1999319692 EMBASE
TITLE: Sensitization of tumor necrosis factor α-resistant human melanoma by tumor-specific in vivo transfer of the gene encoding endothelial monocyte- activating polypeptide II using recombinant vaccinia virus.
AUTHOR: Gnant M.F.X.; Berger A.C.; Huang J.; Puhlmann M.; Wu P.C.; Merino M.J.; Bartlett D.L.; Alexander H.R. Jr.; Libutti S.K.
CORPORATE SOURCE: S.K. Libutti, Surgical Metabolism Section, Surgery Branch, National Cancer Institute, 9000 Rockville Pike, Bethesda, MD 20892, United States
SOURCE: Cancer Research, (15 Sep 1999) 59/18 (4668-4674).
Refs: 69
ISSN: 0008-5472 CODEN: CNREA8
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 013 Dermatology and Venereology
016 Cancer

030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: English
SUMMARY LANGUAGE: English

AB Tumor necrosis factor α (TNF-α) is a proinflammatory cytokine with potent experimental antitumor activity. Its clinical use in cancer treatment is severely limited by its considerable toxicity after systemic administration, and it is currently confined to isolated limb and organ perfusion settings. In this report, we introduce a novel concept of TNF-α- based gene therapy using the TNF-sensitizing properties of endothelial cell monocyte-activating polypeptide **II** ( **EMAP-II**). We hypothesized that transfer of the EMAP-H gene into established TNF-resistant human melanomas would render these tumors sensitive to subsequent systemic TNF-α treatment. To achieve tumor selective gene delivery, we constructed a recombinant vaccinia virus encoding the human **EMAP-II** gene (vvEMAP). In vitro transfection of human melanoma cells led to the production of **EMAP -II** by these cells. Supernatants of vvEMAP-transfected tumor cells mediated the induction of tissue factor in endothelial cells. We characterized the pattern of gene expression after systemic administration of a recombinant vaccinia virus encoding a reporter gene in a murine in vivo model of s.c. human melanoma. Gene expression in tumor tissue was increased 100-fold as compared with normal tissue, providing evidence for tumor-selective gene delivery. Finally, human melanomas in nude mice were sensitized in vivo by transferring the **EMAP-II** gene using vvEMAP. Subsequent systemic administration of TNF-α led to tumor regression and growth **inhibition** of these previously TNF-resistant tumors ($P < 0.05$). This approach using gene therapy to sensitize primarily unresponsive tumors toward TNF-α may enhance the usefulness of TNF-α in clinical treatment strategies by increasing the window for the therapeutic application of the cytokine, thus **reducing** the dose necessary for antitumor responses and subsequently **reduce** toxicity.

L11 ANSWER 11 OF 20 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 1999422800 EMBASE
TITLE: Apoptosis induced by a corneal-endothelium-derived cytokine.
AUTHOR: Liu S.H.; Gottsch J.D.
CORPORATE SOURCE: S.H. Liu, Wilmer Eye Institute, Johns Hopkins Univ. Sch. of Medicine, Baltimore, MD 21287-9142, United States
SOURCE: Investigative Ophthalmology and Visual Science, (1999) 40/13 (3152-3159).
Refs: 30
ISSN: 0146-0404 CODEN: IOVSDA
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 012 Ophthalmology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB PURPOSE. The purpose of this study was to isolate and characterize cDNA clones encoding target proteins for autoantibodies in patients at high risk for transplant rejection. METHODS. A pool of 10 sera from patients at high risk for rejection who had undergone corneal transplantation was used for immunoscreening of an endothelial cDNA library, and the cDNA fragments were subcloned into prokaryotic expression vectors to generate recombinant fusion proteins. Cytotoxicity of recombinant protein was determined by a modified 51Cr-release assay. Apoptosis induced by recombinant protein was determined by fluorescent dye-chromatin fragmentation assay and by TdT-dUTP terminal nick-end labeling (TUNEL) assay. An enzyme-linked immunosorbent assay was used to detect the presence of antibodies to

recombinant protein in the sera of high-risk patients undergoing corneal transplantation and of control subjects. RESULTS. Screening of 500,000 plaques identified six positive clones, one of which demonstrated extensive homology with a novel tumor- derived cytokine termed **endothelial monocyte-activating polypeptide** (EMAP). EMAP was synthesized as a 39-kDa precursor that was proteolytically cleaved to generate an active 22-kDa cytokine. The mature peptide of EMAP alone was capable of inducing the death of cultured endothelial cells, whereas the propeptide was inactive. The protein synthesis **inhibitor** cycloheximide potentiated EMAP-induced apoptosis in endothelial cells. Cell death by apoptosis was evidenced by DNA fragmentation, extensive surface bleb formation, and chromatin condensation. A statistically significant difference was found in the level of antibodies specific to EMAP between patients at high risk for corneal transplant rejection and control subjects ($P < 0.001$). The antibody levels were elevated in patients with severe graft reaction when compared with patients with no graft reaction ($P < 0.001$). CONCLUSIONS. These studies demonstrated that EMAP is a novel protein in corneal endothelial cells that is capable of inducing programmed cell death. Overexpression of this cytokine could initiate endothelial cell damage leading to stromal edema and corneal decompensation.

L11 ANSWER 12 OF 20 MEDLINE on STN
ACCESSION NUMBER: 1999359488 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10430623
TITLE: Endothelial-monocyte activating polypeptide II, a novel antitumor cytokine that suppresses primary and metastatic tumor growth and induces apoptosis in growing endothelial cells.
AUTHOR: Schwarz M A; Kandel J; Brett J; Li J; Hayward J; Schwarz R E; Chappey O; Wautier J L; Chabot J; Lo Gerfo P; Stern D
CORPORATE SOURCE: Department of Pediatrics, Columbia University, College of Physicians and Surgeons, New York 10032, USA..
mschwarz@chla.usc.edu
CONTRACT NUMBER: HL42833 (NHLBI)
KO2 HL03981 (NHLBI)
KO2 HL60061 (NHLBI)
SOURCE: Journal of experimental medicine, **(1999 Aug 2)** 190 (3) 341-54.
Journal code: 2985109R. ISSN: 0022-1007.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990827
Last Updated on STN: 19990827
Entered Medline: 19990819

AB Neovascularization is essential for growth and spread of primary and metastatic tumors. We have identified a novel cytokine, **endothelial-monocyte activating polypeptide** (**EMAP**) **II**, that potently **inhibits** tumor growth, and appears to have antiangiogenic activity. Mice implanted with Matrigel showed an intense local angiogenic response, which EMAP II blocked by 76% ($P < 0.001$). Neovascularization of the mouse cornea was similarly prevented by EMAP II ($P < 0.003$). Intraperitoneally administered **EMAP II** suppressed the growth of primary Lewis lung carcinomas, with a **reduction** in tumor volume of 65% versus controls ($P < 0.003$). Tumors from human breast carcinoma-derived MDA-MB 468 cells were suppressed by >80% in EMAP II-treated animals ($P < 0.005$). In a lung metastasis model, **EMAP II** blocked outgrowth of Lewis lung carcinoma macrometastases; total surface metastases were diminished by 65%, and of the 35% metastases

present, approximately 80% were **inhibited** with maximum diameter <2 mm (P < 0.002 vs. controls). In growing capillary endothelial cultures, EMAP II induced apoptosis in a time- and dose-dependent manner, whereas other cell types were unaffected. These data suggest that EMAP II is a tumor-suppressive mediator with antiangiogenic properties allowing it to target growing endothelium and limit establishment of neovasculature.

L11 ANSWER 13 OF 20 MEDLINE on STN
ACCESSION NUMBER: 1999125902 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9928822
TITLE: Effects of autoantigen and dexamethasone treatment on expression of endothelial-monocyte activating polypeptide II and allograft-inflammatory factor-1 by activated macrophages and microglial cells in lesions of experimental autoimmune encephalomyelitis, neuritis and uveitis.
AUTHOR: Schluesener H J; Seid K; Meyermann R
CORPORATE SOURCE: Institute of Brain Research, University of Tubingen, Germany.
SOURCE: Acta neuropathologica, **(1999 Feb)** 97 (2) 119-26. Journal code: 0412041. ISSN: 0001-6322.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199905
ENTRY DATE: Entered STN: 19990601
Last Updated on STN: 20000303
Entered Medline: 19990518

AB Endothelial-monocyte activating polypeptide II (EMAP II) and allograft-inflammatory factor-1 (AIF-1) are two proteins produced by activated monocytes and microglial cells. We now report expression of these factors during experimental therapy of rat neuroautoimmune diseases. Comparative analysis of two therapeutic strategies, treatment with high doses of recombinant autoantigens or with dexamethasone, revealed unexpected differences. High doses of autoantigen were most effective in experimental autoimmune encephalomyelitis and neuritis (EAE and EAN), but less effective in experimental autoimmune uveitis (EAU). Low and high doses of dexamethasone treatment greatly reduced the severity of EAE, EAN and EAU at day 11, but a relapse was observed between days 21 and 26. Only rather limited expression of EMAP II and AIF-1 is seen in the normal central nervous system (CNS). This constitutive expression is not abolished by dexamethasone treatment. In inflammatory autoimmune lesions of the rat CNS, prominent AIF-1 and EMAP II staining was seen with macrophages and monocytes. In particular, parenchymal microglial cells were now activated to express AIF-1 and EMAP II. In accordance with prevention of neurological signs, histological observations revealed that accumulation of activated monocytes expressing **EMAP II** and AIF-1 in the CNS or peripheral nervous system and the massive expression of these factors by parenchymal microglial cells is **inhibited** by high doses of autoantigen. Dexamethasone prevented or abolished local expression of EMAP II and AIF-1 at days 10-16. However, an acute and severe relapse occurred in encephalomyelitis between days 20-26. In these cases, a smoldering expression of EMAP II and AIF-1 persisting long after cessation of neurological signs was observed. Thus, expression of EMAP II and AIF-1 by infiltrating activated macrophages is a marker of disease activity and expression of these factors could be used to demonstrate 'silent' lesions in the CNS and prolonged microglial cell activation. Apparently, AIF-1 and EMAP II immunoreactivity are tools to stage activation of monocytes and microglial cells in inflammatory lesions.

L11 ANSWER 14 OF 20 MEDLINE on STN
ACCESSION NUMBER: 1998445370 MEDLINE

DOCUMENT NUMBER: PubMed ID: 9770485
TITLE: Regulation of endothelial monocyte-activating polypeptide II release by apoptosis.
AUTHOR: Knies U E; Behrensdorf H A; Mitchell C A; Deutsch U; Risau W; Drexler H C; Clauss M
CORPORATE SOURCE: Department of Molecular Cell Biology, Max-Planck-Institut fur Physiologische und Klinische Forschung, Parkstrasse 1, 61231 Bad Nauheim, Germany.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, **(1998 Oct 13)** 95 (21) 12322-7.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 19990106
Entered Medline: 19981112

AB Endothelial monocyte-activating polypeptide II (EMAP II) is a proinflammatory cytokine and a chemoattractant for monocytes. We show here that, in the mouse embryo, EMAP II mRNA was most abundant at sites of tissue remodeling where many apoptotic cells could be detected by terminal deoxynucleotidyltransferase-mediated dUTP end labeling. Removal of dead cells is known to require macrophages, and these were found to colocalize with areas of EMAP II mRNA expression and programmed cell death. In cultured cells, post-translational processing of pro-EMAP II protein to the mature released EMAP II form (23 kDa) occurred coincidentally with apoptosis. Cleavage of pro-**EMAP II** could be abrogated in cultured cells by using a peptide-based **inhibitor**, which competes with the ASTD cleavage site of pro-**EMAP II**. Our results suggest that the coordinate program of cell death includes activation of a caspase-like activity that initiates the processing of a cytokine responsible for macrophage attraction to the sites of apoptosis.

L11 ANSWER 15 OF 20 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 125:204498 CA
TITLE: Methods and compositions for gene therapy of solid tumors in vivo
INVENTOR(S): Burrows, Francis J.; Fong, Timothy C.; Polo, John M.; Dubensky, Thomas W., Jr.; Jolly, Douglas J.
PATENT ASSIGNEE(S): Chiron Viagene, Inc., USA
SOURCE: PCT Int. Appl., 159 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9621416 | A2 | 19960718 | WO 1995-US16855 | 19951222 <-- |
| WO 9621416 | A3 | 19961010 | | |
| W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| AU 9646082 | A1 | 19960731 | AU 1996-46082 | 19951222 <-- |
| EP 802801 | A2 | 19971029 | EP 1995-944229 | 19951222 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE | | | | |
| JP 2001520503 | T2 | 20011030 | JP 1996-521685 | 19951222 |

PRIORITY APPLN. INFO.: US 1994-368574 A 19941230
WO 1995-US16855 W 19951222

AB The present invention provides compns. and methods for treatment of solid tumors with gene therapy utilizing recombinant viral vectors that express polypeptides which (1) selectively initiate irreversible coagulation of blood in the tumor vasculature, (2) inhibit tumor neovascularization, (3) are capable of activating a non-toxic agent into a toxic agent within the tumor vascular wall causing destruction of the vascular bed, and (4) absorb or metabolize nutrients in the blood being supplied to the tumor. The production of these polypeptides by transduced cells in or adjacent to the blood vessels of the tumor result in the death of tumor cells.

L11 ANSWER 16 OF 20 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 125:112422 CA
TITLE: A novel tumor-derived mediator that sensitizes cytokine-resistant tumors to tumor necrosis factor
AUTHOR(S): Marvin, Michael R.; Libutti, Steven K.; Kayton, Mark; Kao, Janet; Hayward, Joanne; Grikscheit, Tracy; Fan, Yan; Brett, Jerold; Weinberg, A.; et al.
CORPORATE SOURCE: College Physicians and Surgeons, Columbia University, New York, NY, 10032, USA
SOURCE: Journal of Surgical Research (**1996**), 63(1), 248-255
CODEN: JSGRA2; ISSN: 0022-4804
PUBLISHER: Academic
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Therapeutic successes following treatment of murine tumors with tumor necrosis factor-α (TNF) have not been easily applied to clin. oncol. because the concns. of TNF required in humans induces systemic toxicity. This has led the authors to identify mediators which could sensitize tumors to the effects of TNF, permitting administration of lower doses and possible realization of the therapeutic potential of this cytokine. Here is reported the ability of a novel cytokine, endothelial-monocyte-activating polypeptide II (EMAP II), to sensitize initially resistant murine and human tumors to TNF-induced regression employing a murine model. Recombinant (r) EMAP II was purified from Escherichia coli transformed with a plasmid expressing mature EMAP II. The B16 melanoma, raised in C57BL/6 mice, or a human fibrosarcoma (HT-1080), grown in immunocompromised mice, was injected intratumorally with either vehicle or rEMAP II/heat-treated EMAP II (50-100 μg) followed by systemic TNF/heat-treated TNF (5 μg) and assessed for tumor volume, hemorrhage, and histol. appearance. Both the B16 melanoma and the HT-1080 human fibrosarcoma underwent thrombohemorrhagic and acute inflammatory changes concomitant with regression or slowed growth after administration of intratumor EMAP II followed by systemic TNF. Omission or inactivation of either cytokine abrogated this effect. Thus, local treatment of certain tumors with EMAP II results in enhanced susceptibility to TNF-mediated induction of thrombohemorrhage and regression.

L11 ANSWER 17 OF 20 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 123:54152 CA
TITLE: Endothelial-monocyte activating polypeptide II, its human and murine cDNA sequence, and its cytokine activity for host response and tumor regression
INVENTOR(S): Stern, David M.; Clauss, Matthias; Kao, Janet; Kayton, Mark; Libutti, Steven K.
PATENT ASSIGNEE(S): Trustees of Columbia University in the City of New York, USA
SOURCE: PCT Int. Appl., 181 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9509180 | A1 | 19950406 | WO 1994-US11085 | 19940929 <-- |
| W: AU, CA, JP, US | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| US 5641867 | A | 19970624 | US 1993-129456 | 19930929 <-- |
| CA 2172729 | AA | 19950406 | CA 1994-2172729 | 19940929 <-- |
| AU 9479615 | A1 | 19950418 | AU 1994-79615 | 19940929 <-- |
| EP 721463 | A1 | 19960717 | EP 1994-930525 | 19940929 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| JP 09505987 | T2 | 19970617 | JP 1994-510465 | 19940929 <-- |
| US 6228837 | B1 | 20010508 | US 1996-360821 | 19961008 |
| US 2002160957 | A1 | 20021031 | US 2001-851026 | 20010507 |

PRIORITY APPLN. INFO.:
US 1993-129456 A 19930929
WO 1994-US11085 W 19940929
US 1996-360821 A1 19961008

AB A purified endothelial monocyte activating polypeptide (EMAP II) is provided. Further provided are a method of obtaining purified EMAP II, a method of making antibodies to it, and a method for its detection. This invention also provides an effector cell activating protein which contains an amino acid sequence homologous to RIGRIVT and a method of detecting same. This invention also provides a method of treating a tumor in a subject by administering an ED of EMAP II. Thus, EMAP-II was initially identified in the supernatant of murine methylcholanthrene A-induced fibrosarcomas by its capacity to activate host effector cells. Based on its N-terminal protein sequence, a full-length cDNA was cloned which indicates that the precursor of EMAP II is a unique, leaderless, single polypeptide chain with predicted mol. mass .apprx.34 kDa and that the mature form released by Meth A cells corresponds to .apprx.20 kDa. Purified recombinant mature EMAP II activated endothelial cells with resulting elevation of cytosolic free calcium concn, release of von Willebrand factor, induction of tissue factor, and expression of the adhesion mols. E-selectin and P-selectin. Neutrophils exposed to EMAP II demonstrated elevated cytosolic free calcium concentration, peroxidase generation, and chemotaxis. EMAP II also activated mononuclear phagocytes. Systemic infusion of EMAP II into C3H/HeJ or Balb/c mice was associated with systemic toxicity, pulmonary congestion, and the appearance of TNF, interleukin-1 and -6 in the plasma. A single intra-tumor injection of EMAP II into Meth A sarcomas induced acute thrombohemorrhage and partial tumor regression. Local injection of EMAP II into a tumor resistant to the effects of TNF, murine mammary carcinoma, rendered it sensitive to subsequently administered TNF, which resulted in acute thrombohemorrhage and partial regression. Thus, recombinant EMAP II, a tumor-derived cytokine, has properties of a proinflammatory mediator with the capacity to prime the tumor vasculature for a locally destructive process.

L11 ANSWER 18 OF 20 CA 
ACCESSION NUMBER: 121:253396 CA
TITLE: Characterization of a novel tumor-derived cytokine. Endothelial-monocyte activating polypeptide II
AUTHOR(S): Kao, Janet; Houck, Keith; Fan, Yan; Haehnel, Iris; Libutti, Steven K.; Kayton, Mark L.; Grikscheit, Tracy; Chabot, John; Nowygrod, Roman; et al.
CORPORATE SOURCE: College of Physicians and Surgeons, Columbia University, New York, NY, 10032, USA
SOURCE: Journal of Biological Chemistry (**1994**), 269(40), 25106-19
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Endothelial-monocyte activating polypeptide II (EMAP II) was initially identified in the supernatant of murine methylcholanthrene A-induced fibrosarcomas (Meth A) by its capacity to activate host effector cells (Kao, J., Ryan, J., Brett, J., Chen, J., Shen, H., Fan Y-G., Godman, G., Familletti, P., Wang, F., Pan, Y-C., Stern, D., and Clauss M. (1992) J. Biol. Chemical 267, 20239-20247). Based on the NH2-terminal protein sequence, a full-length cDNA has been cloned which indicates that the precursor of EMAP II is a unique, leaderless, single polypeptide chain with predicted mol. mass ≈34 kDa and that the mature form released by Meth A cells corresponds to ≈20 kDa. Purified recombinant mature EMAP II (EMAP II, ≈20 kDa form) activated endothelial cells with resulting elevation of cytosolic free calcium concentration, release of von Willebrand factor, induction of tissue factor, and expression of the adhesion mols. E-selectin and P-selectin. Neutrophils exposed to EMAP II demonstrated elevated cytosolic free calcium concentration, peroxidase generation, and chemotaxis. EMAP II also activated mononuclear phagocytes elevating cytosolic free calcium concentration, inducing tumor necrosis factor-α (TNF) and tissue factor, and stimulating chemotaxis. Systemic infusion of EMAP II into C3H/HeJ or Balb/c mice was associated with systemic toxicity, pulmonary congestion, and the appearance of TNF, interleukin-1 and -6 in the plasma. A single intratumor injection of EMAP II into Meth A sarcomas induced acute thrombohemorrhage and partial tumor regression. Local injection of EMAP II into a tumor resistant to the effects of TNF, murine mammary carcinoma, rendered it sensitive to subsequently administered TNF, which resulted in acute thrombohemorrhage and partial regression. These data suggest that recombinant EMAP II, a tumor-derived cytokine, has properties of a proinflammatory mediator with the capacity to prime the tumor vasculature for a locally destructive process.

L11 ANSWER 19 OF 20 MEDLINE on STN

ACCESSION NUMBER: 94193665 MEDLINE

DOCUMENT NUMBER: PubMed ID: 7545917

TITLE: A peptide derived from the amino terminus of endothelial-monocyte-activating polypeptide II modulates mononuclear and polymorphonuclear leukocyte functions, defines an apparently novel cellular interaction site, and induces an acute inflammatory response.

AUTHOR: Kao J; Fan Y G; Haehnel I; Brett J; Greenberg S; Clauss M; Kayton M; Houck K; Kisiel W; Seljelid R; +

CORPORATE SOURCE: Department of Physiology, Columbia University College of Physicians and Surgeons, New York, New York 10032.

CONTRACT NUMBER: HL21006 (NHLBI)
HL42507 (NHLBI)
HL42833 (NHLBI)
+

SOURCE: Journal of biological chemistry, **(1994 Apr 1)** 269 (13) 9774-82.
Journal code: 2985121R. ISSN: 0021-9258.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

OTHER SOURCE: GENBANK-U10117; GENBANK-U10118

ENTRY MONTH: 199405

ENTRY DATE: Entered STN: 19940511
Last Updated on STN: 19970203
Entered Medline: 19940505

AB Endothelial-monocyte-activating polypeptide II (EMAP II) is a novel mediator isolated from conditioned medium of methylcholanthrene A-induced tumor cells which modulates properties of endothelial cells, mononuclear

phagocytes (MPs), and polymorphonuclear leukocytes (PMNs) in vitro and induces an acute inflammatory response in vivo. A synthetic peptide comprising 15 residues from the N-terminal region (residues 6-20) was shown to induce directional migration of MPs and PMNs, with half-maximal effect at approximately 200-250 pM, whereas a peptide from the C terminus of EMAP II, as well as other irrelevant peptides, were without effect. Modulation of cellular phenotype by EMAP II-derived peptide was suggested by peptide-induced elevation of cytosolic free calcium concentration in fura-2-loaded MPs and PMNs and by stimulation of peroxidase release in PMNs. Consistent with these in vitro data, EMAP II-derived N-terminal peptide-albumin conjugates injected into the mouse footpad elicited inflammatory cell tissue infiltration, whereas albumin alone or EMAP II-derived C-terminal peptide conjugated to albumin incited little response. Binding of 125I-labeled EMAP II-derived peptide (residues 12-20) to MPs was saturable (Kd approximately 200 pM) and was blocked in a dose-dependent manner by the addition of intact EMAP II and unlabeled EMAP II-derived peptides (residues 6-20 and 12-20), whereas interleukin 1, tumor necrosis factor, formyl-methionyl-leucinyl-phenylalanine, or irrelevant peptides were without effect. Cross-linking of 125I-**EMAP II**-derived peptide (residues 12-20) by disuccinimidyl suberate to human MPs demonstrated a band, approximately 73 kDa, on **reduced** sodium dodecyl sulfate-polyacrylamide gel electrophoresis. 125I-**EMAP II**-derived peptide also demonstrated specific binding to human PMNs and murine RAW cells. These data indicate that the N-terminal region of EMAP II defines a biologically active locus of the molecule which interacts with target cells via a potentially novel cellular receptor.

L11 ANSWER 20 OF 20 EMBASE  on STN

ACCESSION NUMBER: 92316014 EMBASE
DOCUMENT NUMBER: 1992316014
TITLE: Endothelial monocyte-activating polypeptide II. A novel tumor-derived polypeptide that activates host-response mechanisms.
AUTHOR: Kao J.; Ryan J.; Brett G.; Chen J.; Shen H.; Fan Y.-G.; Godman G.; Familletti P.C.; Wang F.; Pan Y.-C.E.; Stern D.; Clauss M.
CORPORATE SOURCE: Dept. of Physiology, College of Physicians and Surgeons, Columbia University, 630 W. 168th St.,New York, NY 10032, United States
SOURCE: Journal of Biological Chemistry, (1992) 267/28 (20239-20247).
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB An important means by which tumor cells influence the vasculature is through the production of soluble mediators altering vascular properties. A .simeq.22-kDa polypeptide was purified to homogeneity from conditioned medium of murine methylcholanthrene A (meth A) fibrosarcoma cells by ion-exchange chromatography and preparative sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE), based on its ability to induce tissue factor procoagulant activity in endothelial cells (ECs). The final product migrated as a broad band on **reduced** and nonreduced SDS-PAGE and had a unique amino- terminal sequence. This meth A-derived polypeptide modulated EC coagulant properties through the induction of tissue factor, induced monocyte migration and tissue factor expression, and was also chemotactic for granulocytes. Injection of the

polypeptide into mouse footpads resulted in an inflammatory response with tissue swelling and polymorphonuclear leukocyte infiltration. The ability of this mediator to activate ECs and monocytes has led us to name it **EMAP II** (**endothelial monocyte-activating polypeptide**). **EMAP II** is distinct from a previously described .simeq.40-kDa meth A-derived polypeptide termed EMAP I. Through its potential to activate host effector mechanisms, **EMAP II** could contribute to the biology of immunogenic tumors, such as the meth A fibrosarcoma.